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Therapeutic Vaccination

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Fort Detrick, Maryland 21702-5012

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13. SUPPLEMENTARY NOTES					
14. ABSTRACT Molecular targets to facilitate early detection and preventative therapy for women at high risk for breast cancer have not been characterized. Two recently characterized intracellular enzymes -- human telomerase reverse transcriptase (hTERT) and the cytochrome P450 isoform 1B1 (CYP1B1), each overexpressed in >90% of invasive breast cancers but rarely found in normal tissue -- may fill this gap. Such targets, if found at the earliest time of malignant transformation, may be ideally suited not only for early detection but also cancer prevention by vaccination. A growing clinical experience in advanced cancer patients has underscored the safety and feasibility of vaccination strategies. The universal expression of hTERT and CYP1B1 provide an opportunity for both early detection and cancer vaccination. Objective/Hypothesis: We hypothesize that immunologic responses can be elicited in advanced breast cancer patients using vaccines incorporating hTERT, providing a safety and feasibility platform for ultimately vaccinating women at high risk for breast cancer. Although we have not found ductal lavage a feasible strategy for the detection of tumor antigens, we have made significant progress on vaccination strategies in women with metastatic breast cancer.					
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Progress Report
Department of Defense Physician-Scientist Award
Universal Breast Cancer Antigens as Targets Linking Early Detection and Therapeutic Vaccination

Susan M. Domchek, MD

October 8, 2006

SPECIFIC AIMS OF THE PROJECT

- 1. Evaluation of molecular markers in ductal lavage fluid from BRCA1 and BRCA2 mutation carriers**
- 2. Determine the safety and feasibility of vaccinating advanced breast cancer patients with hTERT peptide, assessing the generation of hTERT-specific immunity. Explore the role of intravenous cyclophosphamide prior to hTERT vaccination in boosting vaccine response by depleting regulatory T cells.**

A. INTRODUCTION

This grant supports studies to understand the potential of universal tumor antigens for cancer immunotherapy, with a particular focus on the characterization of the human telomerase reverse transcriptase (hTERT) as tumor antigen. Telomerase is expressed by >90% of all human breast cancers but absent in most normal cells. Telomerase function has been directly linked to oncogenesis and its inhibition in telomerase-positive human tumors leads to growth arrest.

Following a series of published in vitro preclinical experiments, we are now testing the hypothesis of telomerase as a tumor rejection antigen in vivo in humans. After our past work in completing the dose escalation portion of the hTERT vaccine trial, as well as enrolling additional patients on the optimal dose level, this year we proceeded with work evaluating intravenous cyclophosphamide prior to hTERT vaccination in an attempt to boost vaccine response by depleting regulatory T cells. Funding has been obtained to continue this work beyond the end of the Department of Defense grant.

B. BODY

Aim 1: Evaluation of molecular markers in ductal lavage fluid from BRCA1 and BRCA2 mutation carriers

Increasing data have demonstrated significant limitations regarding ductal lavage, particularly in *BRCA1/2* mutation carriers. Data by several groups have demonstrated that fluid yielding ducts are much less common in women following oophorectomy or taking selective estrogen receptor modulations (SERMS), situations which apply to the majority of *BRCA1* and *BRCA2* mutation carriers. In addition, the cellular yield of non-fluid yielding ducts is significantly lower than in fluid yielding ducts. Finally, ductal lavage has a low sensitivity for the detection of malignancy as examined by ductal lavage prior to mastectomy for known cancers. As the

majority of our *BRCA1/2* carriers have had oophorectomy, it is our opinion that the value of ductal lavage is quite limited and the approach not feasible. Therefore, we examined the value of oophorectomy on mortality in *BRCA1/2* mutation carriers. We felt that this was a much better use of DOD resources.

In the primary analysis of this study, which was published in *Lancet Oncology*, we examined 426 women unaffected with either breast or ovarian cancer at the start of study entry. Study participants who choose to undergo oophorectomy were age-matched to those who did not. At a median follow-up of 2-3 years, PO led to a risk reduction for breast cancer (HR 0.36, 0.20-0.67) and ovarian cancer (HR 0.11, 0.03-0.47) consistent with prior reports. In addition, a reduction in breast cancer specific mortality (HR 0.10, 0.02-0.71), ovarian cancer specific mortality (HR 0.05, 0.01-0.46) and overall mortality (HR 0.24, 0.08-0.71) were also seen. Median follow-up time in this study is short, and the sample size still relatively small. Despite the limitations, these data provide further evidence that PO in *BRCA1/2* mutation carriers is of benefit.

Aim 2: Determine the safety and feasibility of vaccinating advanced breast cancer patients with hTERT peptide, assessing the generation of hTERT-specific immunity. Explore the role of intravenous cyclophosphamide prior to hTERT vaccination in boosting vaccine response by depleting regulatory T cells.

We have vaccinated 17 HLA-A2+ women with metastatic breast cancer subcutaneously with various doses of hTERT I540 peptide emulsified in Montanide adjuvant and administered with granulocyte macrophage colony-stimulating factor (GM-CSF) for up to eight vaccinations. Based on *in vitro* analyses performed on peripheral blood obtained before and after vaccination, 11 of 17 patients were found to have responded immunologically to the vaccine. For immunological responders after vaccination, clear populations of hTERT tetramer+ CD8+ T cells were identified following a single round of *in vitro* peptide stimulation (median percentage of tetramer+ CD8+ T cells was 0.98%, compared to <0.10% of such cells at baseline in these patients or in immunological non-responders at any time point). T cells were specific for hTERT peptide and recognized telomerase-positive, HLA-A2+ (but not HLA-A2-negative) carcinoma cells, as shown by IFN-gamma production and cytotoxicity assays. For three patients undergoing tumor biopsy, hTERT-specific CD8+ tumor infiltrating lymphocytes (TIL) were observed by tetramer analysis after, but not before, vaccination, measuring >5% tetramer+ cells among CD8+ T cells. In two patients, TILs were associated with marked tumor necrosis. The most common adverse events were Grade 1-2 injection site reactions and a syndrome of tumor pain or tumor-site pruritis after vaccination.

By a landmark survival analysis, we investigated the association of the induction of hTERT-specific CTL in peripheral blood and survival. For 14 patients who received at least four vaccines, the landmark was defined as the immune response status after the fourth vaccination (median on study day 70, range 55-78). The median survival among six non-responders was 12.6 months (95% CI = 6.0-19.2 months) whereas the median survival of eight immunological responders has not yet been reached at a median follow-up of 15.7 months (range 0.9⁺ to 22.3⁺ months). No other clinical parameter we investigated in this way correlates with survival, including age, hormone status, her2/neu status, prior treatment, or time since initial diagnosis.

Moreover, we also used tetramer analysis to track responses to the CMV control peptide in the vaccine. We found that by landmark analysis there was no correlation between overall survival and CMV response 1 month after the fourth vaccination.

These results suggest that telomerase vaccination of patients with metastatic breast cancer induces hTERT-specific T cells that may impact overall survival. Interestingly, the primary immune assay used as the endpoint in this survival analysis was tetramer labeling.

This year we have treated 5 patients with intravenous cyclophosphamide prior to the administration of hTERT vaccine to assess whether such an intervention might enhance immune response. Preliminary data does not support this hypothesis, although detailed immunological assessments are underway.

KEY RESEARCH ACCOMPLISHMENTS

1. Completion of optimal dose portion of protocol UPCC 11102
2. Completion of landmark analysis for patients undergoing on UPCC 11102 demonstrating a correlation of survival in immune responders to hTERT.
3. Selected for oral presentation at the American Association of Clinical Research annual meeting in 2006 entitled: "Telomerase vaccination of metastatic breast cancer patients induces antigen-specific tumor infiltrating lymphocytes and tumor necrosis"
4. Four patients treated with intravenous cyclophosphamide as an immune modulator prior to hTERT vaccination

REPORTABLE OUTCOMES:

A. Publications During This Funding Period (2005-2006)

1. Danet-Desnoyers GA, Luongo JL, Bonnet DA, Domchek SM, Vonderheide RH: Telomerase vaccination has no detectable effect on SCID-repopulating and colony-forming activities in the bone marrow of cancer patients. Experimental Hematology Vol. 33: 1275-80, 2005.
2. Halbert C, Brewster K, Collier A, Smith C, Kessler L, Weathers B, Stopfer J, Domchek S, and Wiley EP: Recruiting African American Women to Participate in Hereditary Breast Cancer Research. Journal of Clinical Oncology Vol. 23: 7957-73, 2005.
3. Rebbeck TR, Friebel R, Wagner R, Lynch HT, Garber JE, Daly MB, Isaacs C, Olopade O, Neuhausen SL, Van't Veer L, Eeles R, Evans F, Tomlinson G, Matloff E, Narod SA, Eisen A, Domchek S, Armstrong K, Weber BL: Effect of short term hormone replacement therapy on breast cancer risk reduction after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers. Journal of Clinical Oncology Vol. 23: 7804-10, 2005.
4. Domchek SM and Weber BL. Guidelines for genetic counseling, testing and referral in North America. Chapter in *Risk Assessment and Management in Cancer Genetics*. Eds. Lalloo F, Kerr B, Friedman JM, Evans DGR. 2005.

75. Stopfer JE and Domchek SM: Commentary: Clinical Management of BRCA1/2 mutation carriers. Oncology Vol. 19: 1462-5, 2005.
6. Domchek SM, Stopfer JE, Rebbeck TR : Bilateral risk-reducing oophorectomy in BRCA1 and BRCA2 mutation carriers. J Natl Comp Can Netw Vol. 4: 177-182, 2006.
7. Domchek SM, Armstrong K, Weber BL: Clinical Management of BRCA1 and BRCA2 mutation carriers. Nature Clinical Practice Oncology Vol. 3: 2-3, 2006.
8. Charles S, Kessler L, Stopfer J, Domchek S, Halbert C: Satisfaction with Genetic Counseling for BRCA1 and BRCA2 Mutations among African American Women. Patient Education and Counseling March 2006.
9. Kessler L, Domchek S, Stopfer J, Halbert C: BRCA1 and BRCA2 Risk Perceptions among African American Women at Increased Risk for Hereditary Breast-Ovarian Cancer. Community Genetics March 2006.
10. Domchek SM, Friebel R, Neuhausen SL, Wagner R, Evans G, Isaacs C, Garber JE, Daly MB, Eeles R, Matloff E, Tomlinson G, Van't Beer L, Lynch HT, Olopade OI, Narod SA, Weber BL, Rebbeck TR. : Reduction in short-term mortality after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers. Lancet Oncology 7(3): 223-9, 2006.
11. Hughes Halbert C, Kessler L, Stopfer J, Domchek S, Wileyto EP: Low rates of acceptance of BRCA1 and BRCA2 test results among African American women at increased risk of hereditary breast-ovarian cancer. Genetics in Medicine Vol. in press, 2006.
12. Brooks GA, Stopfer JE, Erlichman J, Davidson R, Nathanson KL, Domchek SM: Childhood cancer in families with and without BRCA1 or BRCA2 mutations ascertained at a high-risk breast cancer clinic. Cancer Biology and Therapy Vol. in press, 2006.
13. Domchek SM and Weber BL: Clinical management of BRCA1 and BRCA2 mutations carriers. Oncogene Vol. in press, 2006.

B. Abstracts

1. Domchek SM, Fox KR, Recio A, Schuchter LM, Davidson R, DeMichele A, Feldman MD, Vonderheide RH. "Immunological and clinical outcomes following telomerase peptide vaccination in patients with metastatic breast cancer" Oral Presentaion, AACR, Washington DC, 2006

C. Funding

Dr. Domchek is a co-investigator on a RO1 which was funded this year. This grant permits the evaluation of I540 peptide vaccination in combination with anti-CD25 mAb in a further attempt to boost immune response by depleting regulatory T cells. The principle investigator on the grant is Dr. Robert Vonderheide, and the grant number is Ro1 CA111377-01A1. Dr. Domchek will be the principle investigator on the clinical trial which will be part of the grant. In addition, Dr. Domchek is the clinical PI of a project entitled, "Telomerase Immunotherapy in Breast Cancer" submitted as part of a PENN/Fox Chase Cancer Center SPORE application. Dr. Domchek's work in breast cancer genetics has resulted in a Cancer Genetics Network Contract through the National Cancer Institute as the University of Pennsylvania site PI. Finally, Dr. Domchek is the lead clinical investigator on two RO1's led by Dr. Timothy Rebbeck (RO1 CA102776 and RO1 CA083855). The first of these grants is examining the impact of prophylactic surgery on *BRCA1/2* mutation carriers, with particular attention to

tumor phenotype as well as interaction with hormonal therapy use. The second study is focused on modifier genes in *BRCA1/2* mutation carriers.

CONCLUSIONS

Data thus far from our current trial suggest that telomerase peptide vaccination is biologically active and leads to in vivo immune recognition of carcinoma by effector lymphocytes and tumor necrosis. This has great potential for biological therapy of breast cancer and required further exploration. If hTERT expression can be found in women at high risk for breast cancer, this may represent a marker to be used to target candidates for vaccination in the future.

REFERENCES (See “Publications” in “Reportable Outcomes”)

APPENDICES

1. Domchek CV

UNIVERSITY OF PENNSYLVANIA - SCHOOL OF MEDICINE
Curriculum Vitae

Date: 10/26/2006

Susan M. Domchek

Address: 14 Penn Tower
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University of Pennsylvania
3400 Spruce Street

Philadelphia, PA 19104 USA

If you are not a U.S. citizen or holder of a permanent visa, please indicate the type of visa you have:
none (U.S. citizen)

Education:

1990	BA	Dartmouth College, Hanover, NH (Engineering Sciences)
1994		Oxford University, England (English Literature)
1995	MD	Harvard Medical School, Boston, MA

Postgraduate Training and Fellowship Appointments:

1995-1996	Intern, Internal Medicine, Massachusetts General Hospital, Boston, MA
1996-1998	Resident, Internal Medicine, Massachusetts General Hospital, Boston, MA
1998-2001	Clinical Fellow in Hematology and Oncology, Dana-Farber Cancer Institute, Boston, MA
2000	Chief Medical Resident, Massachusetts General Hospital, Boston, MA

Military Service:

[none]

Faculty Appointments:

2000-2001	Instructor in Medicine, Harvard University
2001-present	Assistant Professor of Medicine at the Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine

Hospital and/or Administrative Appointments:

2005-present	Director, Cancer Risk Evaluation Program, Abramson Cancer Center, University of Pennsylvania
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Other Appointments:

[none]

Specialty Certification:

1998	American Board of Internal Medicine
2001	American Board of Internal Medicine: Medical Oncology

Licensure:

1998	Massachusetts
2001	Pennsylvania

Awards, Honors and Membership in Honorary Societies:

1989	Choate Scholar, Dartmouth College
1989	Phi Beta Kappa, Dartmouth College
1990	Summa cum laude, Dartmouth College
1993	Marshall Scholar, Oxford University

1995	Magna cum laude, Harvard Medical School
2000	Chief Medical Resident, Massachusetts General Hospital
2001	Landenberger Scholar, University of Pennsylvania
2002-present	Ann B. Young Assistant Professor in Cancer Research, University of Pennsylvania
2002-2005	Tracey Starr Award
2003-2006	Department of Defense, Physician Scientist Award

Memberships in Professional and Scientific Societies and Other Professional Activities:

American Society of Clinical Oncology (Member, 1999-present)

Editorial Positions:

2000-present	Ad Hoc reviewer, Cancer
2001-present	Ad Hoc reviewer, Journal of Clinical Oncology
2002-present	Ad Hoc reviewer, Journal of Medical Genetics
2002-present	Ad Hoc reviewer, New England Journal of Medicine
2002-present	Ad Hoc reviewer, Clinical Cancer Research
2003-present	Ad Hoc reviewer, Journal of General Internal Medicine
2005-present	Ad Hoc reviewer, Breast Journal

Academic and Institutional Committees:

1999-2000	Member, Internship Selection Committee, Massachusetts General Hospital
2000-2001	Member, Teaching and Training Council, Internal Medicine Residency, Massachusetts General Hospital
2000-2001	Member, Training Program Council, Internal Medicine Residency, Massachusetts General Hospital
2003	Member, Educational Taskforce for Department of Medicine Strategic Planning Initiative, University of Pennsylvania
2006-present	Member, GEC Executive Committee, School of Medicine, University of Pennsylvania
2006-present	Member, Obstetrics and Gynecology Strategic Planning Committee, University of Pennsylvania

Major Academic and Clinical Teaching Responsibilities:

2001-present	Assistant Professor of Medicine, University of Pennsylvania •Serve as inpatient attending for four weeks a year, supervising team of fellows, residents, interns and medical students •Serve as inpatient oncology consult four weeks a year, supervising oncology fellows •Preceptor to medical students and residents in outpatient clinic •Preceptor to residents in the Women's Health Elective
2002-present	"Cancer screening trials", Educational series for medical oncology fellows
2003-2006	"Breast cancer genetics", Medical student, endocrinology course. Yearly lecture
2003	"Tamoxifen decision-making", Medical student decision making course

Lectures by Invitation (Last 5 years):

Feb, 2001	"Breast cancer", Massachusetts General Hospital Medical Housestaff lecture series, Boston, MA
Mar, 2001	Harvard Medical Student Subinternship teaching series, monthly presentation, Boston, MA
May, 2001	"Breast cancer, risk and prevention", Newton-Wellesley Hospital, Newton, MA
Jun, 2001	"Hormonal replacement therapy and the risk of breast cancer", Living Well series, Dana-Farber Cancer Institute, Boston, MA
Jul, 2001	"Hormonal therapies in breast cancer", Educational series for radiation oncology residents, Dana-Farber Cancer Institute, Boston, MA

Sep, 2001	"Breast cancer", Massachusetts General Hospital Medical Housestaff lecture series. Boston, MA
Sep, 2002	"Ductal lavage for the detection of breast cancer: how it works and what's the evidence?", Changing Concepts in Breast Cancer 2002 Conference, University of Pennsylvania, Philadelphia, PA
Oct, 2002	"Ductal lavage", Life After Breast Cancer, University of Pennsylvania, Philadelphia, PA
Oct, 2002	"What is a clinical trial?", Pennsylvania Breast Cancer Coalition, Harrisburg, PA
Oct, 2002	"Breast cancer genetics: who to test and how to manage", Moravian College, Bethlehem, PA
Oct, 2002	"Breast cancer: risk, screening, prevention and management", Moravian College, Bethlehem, PA
Nov, 2002	"Hormone replacement therapy and breast cancer risk", FOCUS panel discussion, University of Pennsylvania, Philadelphia, PA
Jan, 2003	"Management of BRCA1 and BRCA2 mutation carriers", San Antonio Update, Sponsored by Baylor College of Medicine, Washington D.C.
Jun, 2003	"Update on breast cancer susceptibility genes". Medical Grand Rounds, Chester County Hospital, West Chester, PA.
Aug, 2003	"Breast, ovarian and colon cancer genetics", Medical Grand Rounds, Pocono Medical Center, East Stroudsburg, PA
Sep, 2003	"Breast cancer genetics: Who to test and how to manage", Medical Grand Rounds, Lancaster General Hospital, Lancaster, PA
Sep, 2003	"Breast cancer genetics", Life After Breast Cancer Conference, University of Pennsylvania, Philadelphia, PA
Jan, 2004	"Breast cancer genetics", Medical Grand Rounds, St. Joseph's Hospital, Reading, PA
May, 2004	"Risk models in clinical practice", National Cancer Institute Risk Modeling Meeting, Washington, D.C.
May, 2004	"Update in adjuvant therapy for breast cancer", Teich Lecture, Beth-Israel Medical Center, New York, NY
Jun, 2004	"ASCO update: Breast cancer prevention, detection and genetics", University of Pennsylvania, Philadelphia, PA
Sep, 2004	"Breast cancer genetics update", Life After Breast Cancer Conference, Philadelphia, PA
Oct, 2004	"Breast cancer overview", Moravian College, Bethlehem, PA
Jan, 2005	"Telomerase immunotherapy of breast cancer", Breast Cancer Think Tank 15, Cuacao, Dutch Antilles
Apr, 2005	"Genetics and women at high risk for breast cancer", at the 1st Annual Women's Health Summit sponsored by the Cleveland Clinical Foundation Women's Health Center
Apr, 2005	"An update on breast cancer genetics", Changing Concepts in Breast Cancer Conference, University of Pennsylvania CME Symposium, Philadelphia, PA
Apr, 2005	"Hereditary breast and ovarian cancer syndroms" at the 1st Annual Women's Health Summit, sponsored by the Cleveland Clinic Foundation Women's Health Center, Cleveland, OH
Apr, 2005	"Genetic Susceptibility and breast cancer", New Strategies in Breast Cancer Conference 2005, Center for Biomedical Continuing Education, Philadelphia, PA
May, 2005	"How to write a clinical trial", Educational Session at the American Society of Clinical Oncology Annual Meeting, Orlando, FL
Oct, 2005	"Clinical management of BRCA1 and BRCA2 mutation carriers", OB/GYN Grand Rounds, University of Pennsylvania, Philadelphia, PA
Oct, 2005	"Genetics Update", Breast Cancer: Early Detection is the Key Conference, Pennsylvania Hospital, Philadelphia, PA
Apr, 2006	"Genetic susceptibility to breast cancer", Continuing Medical Education Course. Philadelphia, PA
Apr, 2006	"History of Breast Cancer", Pennsylvania Hospital, Philadelphia, PA

Apr, 2006	"Breast Cancer Genetics", The Second Annual Helene Madeira Breast Cancer Symposium. Lankenau Hospital, Wynnewood, PA
Jun, 2006	"ASCO Update: Screening, Prevention and Genetics", Philadelphia, PA
Jun, 2006	"Low penetrance genes and breast cancer: a clinical perspective", American Society of Clinical Oncology Education Session, Atlanta GA
Jul, 2006	"Genetic Susceptibility to Breast Cancer", Oncology Seminar, Virginia Commonwealth University, Richmond, VA

Organizing Roles in Scientific Meetings:

May, 2005	Planning Committee Member, Education Committee, Tumor Biology and Genetics, American Society of Clinical Oncology Annual Meeting Orlando, FL
May, 2005	Chairperson, "Risk modifiers in hereditary cancer syndromes", American Society of Clinical Oncology Annual Meeting Orlando, FL
Jun, 2006	Planning Committee Member, Education Committee, Tumor Biology and Genetics, American Society of Clinical Oncology Annual Meeting Atlanta, GA
Jun, 2006	Chairperson, Cancer Genetics Education Committee, American Society of Clinical Oncology Atlanta, GA

Bibliography:

Research Publications, peer reviewed (print or other media):

1. Domchek SM, Auger KR, Chatterjee S, Burke TR Jr, Shoelson SE: Inhibition of SH2 domain/phosphoprotein association by a nonhydrolyzable phosphonopeptide. Biochemistry Vol. 31: 9865-9870, 1992.
2. Piccione E, Case RD, Domchek SM, Hu P, Chaudhuri M, Backer JM, Schlessinger J, Shoelson SE: Phosphatidylinositol 3-kinase p85 SH2 domain specificity defined by direct phosphopeptide/SH2 domain binding. Biochemistry Vol. 32: 3197-3202, 1993.
3. Domchek SM, Younger J, Finkelstein DM, Seiden MV: Predictors of skeletal complications in metastatic breast cancer. Cancer Vol. 89: 363-368, 2000.
4. Domchek SM, Hecht JL, Fleming MD, Pinkus GS, Canellos GP: Lymphomas of the breast: primary and secondary involvement. Cancer Vol. 94: 6-13, 2002.
5. Bendell JC, Domchek SM, Burstein HJ, Harris LN, Younger J, Kuter I, Bunnell C, Rue M, Gelman R, Winer EP: Central nervous system metastases in women who receive trastuzumab-based therapy for metastatic breast cancer. Cancer Vol. 97: 2972-7, 2003.
6. Domchek SM, Eisen A, Calzone K, Stopfer J, Blackwood A, Weber BL: Application of breast cancer risk prediction models in clinical practice. Journal of Clinical Oncology Vol. 21: 593-601, 2003.
7. Huang J, Domchek SM, Brose MS, Rebbeck TR, Nathanson KL, Weber BL: Germline CHEK2*1100delC mutations in breast cancer patients with multiple primary cancers. Am J Hum Gen Vol. 41: e120, 2004.
8. Vonderheide RH, Domchek SM, Schultze J, George DJ, Hoar KM, Chen D, Stephens KF, Masutomi, K, Loda M, Xia Z, Anderson KS, Hahn WC, Nadler LN: Vaccination of cancer patients against telomerase induces functional anti-tumor CD8+ T lymphocytes Clinical Cancer Research Vol. 10: 828-39, 2004.

9. Danet-Desnoyers GA, Luongo JL, Bonnet DA, Domchek SM, Vonderheide RH: Telomerase vaccination has no detectable effect on SCID-repopulating and colony-forming activities in the bone marrow of cancer patients. Experimental Hematology Vol. 33: 1275-80, 2005.
10. Domchek SM, Merillat S, Tigges J, Tweed AJ, Weinar M, Stopfer J, Weber BL: Sex ratio skewing of offspring in families with hereditary susceptibility to breast cancer. J Med Genet Vol. 42: 511-13, 2005.
11. Gurmankin AD, Domchek SM, Stopfer J, Fels C, Armstrong K: Patients' resistance to risk information in genetic counseling for BRCA1/2. Archives of Int Med. Vol. 165: 523-9, 2005.
12. Halbert C, Brewster K, Collier A, Smith C, Kessler L, Weathers B, Stopfer J, Domchek S, and Wiley EP: Recruiting African American Women to Participate in Hereditary Breast Cancer Research. Journal of Clinical Oncology Vol. 23: 7957-73, 2005.
13. Peters N, Domchek SM, Rose A, Polis R, Stopfer J, Armstrong K: Knowledge, attitudes and utilization of BRCA1/2 testing among women with early onset breast cancer. Genetic Testing Vol. 9: 48-53, 2005.
14. Rebbeck TR, Friebel R, Wagner R, Lynch HT, Garber JE, Daly MB, Isaacs C, Olopade O, Neuhausen SL, Van't Veer L, Eeles R, Evans F, Tomlinson G, Matloff E, Narod SA, Eisen A, Domchek S, Armstrong K, Weber BL: Effect of short term hormone replacement therapy on breast cancer risk reduction after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers. Journal of Clinical Oncology Vol. 23: 7804-10, 2005.
15. Schwartz J, Domchek SM, Hwang W, Fox K: Evaluation of anemia, neutropenia, and skin toxicities in standard or dose-dense doxorubicin/cyclophosphamide (AC)-paclitaxel or docetaxel adjuvant chemotherapy in breast cancer. Annals of Oncology Vol. 16: 247-52, 2005.
16. Charles S, Kessler L, Stopfer J, Domchek S, Halbert C: Satisfaction with Genetic Counseling for BRCA1 and BRCA2 Mutations among African American Women. Patient Education and Counseling March 2006.
17. Kessler L, Domchek S, Stopfer J, Halbert C: BRCA1 and BRCA2 Risk Perceptions among African American Women at Increased Risk for Hereditary Breast-Ovarian Cancer. Community Genetics March 2006.
18. Brooks GA, Stopfer JE, Erlichman J, Davidson R, Nathanson KL, Domchek SM: Childhood cancer in families with and without BRCA1 or BRCA2 mutations ascertained at a high-risk breast cancer clinic. Cancer Biology and Therapy Vol. 5, 2006.
19. Domchek SM, Friebel R, Neuhausen SL, Wagner R, Evans G, Isaacs C, Garber JE, Daly MB, Eeles R, Matloff E, Tomlinson G, Van't Beer L, Lynch HT, Olopade OI, Narod SA, Weber BL, Rebbeck TR. : Reduction in short-term mortality after bilateral prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers. Lancet Oncology 7(3): 223-9, 2006.
20. Hughes Halbert C, Kessler L, Stopfer J, Domchek S, Wileyto EP: Low rates of acceptance of BRCA1 and BRCA2 test results among African American women at increased risk of hereditary breast-ovarian cancer. Genetics in Medicine Vol. 8: 576-82, 2006.
21. Hughes Halbert C, Kessler L, Wileyto EP, Weathers B, Stopfer J, Domchek S, Collier A, Brewster K: Breast cancer screening behaviors among African American women with a strong family history of breast cancer. Preventative Medicine Vol. July, 2006.

22. Narod SA, Lubinski J, Ghadirian P, Lynch HT, Moller P, Foukles WD, Rosen B, Kim-Sing C, Isaacs C, Domchek S, Sun P: Screening mammography and risk of breast cancer in BRCA1 and BRCA2 mutation carriers: a case-control study. Lancet Oncology Vol. 7: 360-2, 2006.

Research Publications, peer-reviewed reviews:

1. Domchek SM: Invited Commentary: The utility of ductal lavage in breast cancer detection and risk assessment. Breast Cancer Research Vol. 4: 51-53, 2002.
2. Domchek SM and Weber BL: Clinical management of BRCA1 and BRCA2 mutations carriers. Oncogene Vol. 25: 5825-31, 2006.
3. Domchek SM, Armstrong K, Weber BL: Clinical Management of BRCA1 and BRCA2 mutation carriers. Nature Clinical Practice Oncology Vol. 3: 2-3, 2006.

Contributions to peer-reviewed clinical research publications, participation cited but not by authorship:

[none]

Research Publications, non-peer reviewed:

[none]

Abstracts (Last 3 years):

1. Domchek SM, Fox KR, Recio A, Schuchter LM, Davidson R, DeMichele A, Feldman MD, Vonderheide RH: Telomerase vaccination of metastatic breast cancer patients induces antigen-specific tumor infiltrating lymphocytes and tumor necrosis Selected Oral Abstract Presentation, Department of Defense Era of Hope Meeting, Philadelphia, PA 2005.
2. Domchek SM, Fox KR, Recio A, Schuchter LM, Davidson R, DeMichele A, Feldman MD, Vonderheide RH: Telomerase vaccination of metastatic breast cancer patients induces antigen-specific tumor infiltrating lymphocytes and tumor necrosis Selected Oral Abstract Presentation, American Society of Clinical Oncology, Orlando, FL 2005.
3. Herold CI, Goldfeder KL, Tigges J, Stopfer JE, Weber BL, Domchek SM: Factors that influence genetic testing outcomes in breast/ovarian families. American Society of Clinical Oncology 2005.
4. Armstrong K, Gray S, Domchek S: Internet use is associated with utilization of genetic counseling for BRCA1/2 mutations in women with a family history of breast or ovarian cancer. American Society of Clinical Oncology 2006.
5. Kauff ND, Domchek SM, Friegel TM, Lee JB, Roth R, Robson ME, Barakat RR, Norton L, Offit K, Rebbeck TR: Multi-center prospective analysis of risk-reducing salpingo-oophorectomy to prevent BRCA-associated breast and ovarian cancer. American Society of Clinical Oncology, Selected Oral Presentation 2006.
6. Tchou J, Sonnad S, Sargen M, Weber B, Nathanson K, Domchek S: Contralateral prophylactic mastectomy in affected carriers of deleterious BRCA1 or BRCA2 mutations: does timing of genetic testing matter? American Society of Clinical Oncology 2006.

Editorials, Reviews, Chapters, including participation in committee reports (print or other media):

1. Domchek SM and Garber JE: Genetic Testing for Breast Cancer. Principles & Practice of Oncology: Updates Vol. 15: 1-15, 2001.
2. Domchek SM and Weber BL: Advances in breast cancer biology. Current Opinions in Oncology Vol. 14: 589-593, 2002.
3. Domchek SM: Chemoprevention in BRCA1 and BRCA2 mutation carriers. Seminars in Breast Disease Vol. 6: 30-33, 2003.

4. Domchek SM and Weber BL: Inherited Genetic Factors in Breast Cancer. Diseases of the Breast. Harris J, Lippman M, Morrow M, Osborne CK (eds.). Lippincott Williams and Williams, Page: 277-303, 2004.
5. Stein S, DeMichele A, Domchek S, Fox K: Gemcitabine and trastuzumab combinations for patients with metastatic breast cancer overexpressing HER2/neu. Clinical Breast Cancer Vol. 4: S117-120, 2004.
6. Stein S, DeMichele A, Domchek S, Fox K: Progress in Medical Oncology. Emergency Medicine Vol. 36: 11-19, 2004.
7. Domchek SM and Weber BL: Guidelines for genetic counseling, testing and referral in North America. Chapter in Risk Assessment and Management in Cancer Genetics. Laloo F, Kerr B, Friedman JM, Evans DGR (eds.). Oxford University Press, Page: 23-30, 2005.
8. Rebbeck TR, Stopfer JE, Domchek SM: Commentary: Use of hormone replacement therapy after bilateral risk-reducing oophorectomy in BRCA1 and BRCA2 mutation carriers Hereditary Cancer in Clinical Practice Vol. 3: 91-93, 2005.
9. Schachter M and Domchek SM: Update in chemoprevention in BRCA1 and BRCA2 mutation carriers. Breast Cancer Online Vol. 8: e47, 2005.
10. Stopfer JE and Domchek SM: Commentary: Clinical Management of BRCA1/2 mutation carriers. Oncology Vol. 19: 1462-5, 2005.
11. Domchek SM, Stopfer JE, Rebbeck TR : Bilateral risk-reducing oophorectomy in BRCA1 and BRCA2 mutation carriers. J Natl Comp Can Netw Vol. 4: 177-182, 2006.

Books:

[none]

Alternative Media:

[none]

Patents:

[none]